NPRL2 gene

NPR2-like, GATOR1 complex subunit

Normal Function

The *NPRL2* gene provides instructions for making a protein that is one piece of a group of proteins (complex) called GATOR1. This complex is found in cells throughout the body, where it regulates a signaling pathway called the mTOR pathway. The mTOR pathway is involved in cell growth and division (proliferation), the survival of cells, and the creation (synthesis) of new proteins. The role of the GATOR1 complex is to block this pathway by inhibiting (stopping) the activity of a complex called mTOR complex 1 (mTORC1) that is integral to the mTOR pathway.

In the brain, the mTOR pathway regulates many processes, including the growth and development of nerve cells and their ability to change and adapt over time (plasticity).

Health Conditions Related to Genetic Changes

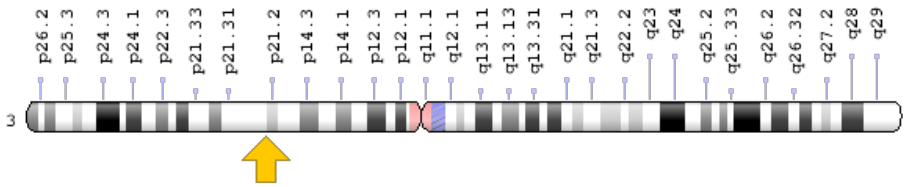
familial focal epilepsy with variable foci

At least 6 *NPRL2* gene mutations have been found to cause familial focal epilepsy with variable foci (FFEVF), which is an uncommon form of recurrent seizures (epilepsy) that runs in families. Most of these mutations lead to the production of an abnormally short, nonfunctional protein. As a result, formation of normal GATOR1 complex is reduced, leading to overactivity of mTORC1 and excessive signaling of the mTOR pathway. It is not clear how an abnormally active mTOR pathway leads to the seizures of FFEVF. Research suggests that increased mTOR pathway signaling in the brain leads to changes in the connections between nerve cells (synapses) and increased activation (excitation) of nerve cells, which can cause seizures.

Chromosomal Location

Cytogenetic Location: 3p21.31, which is the short (p) arm of chromosome 3 at position 21.31

Molecular Location: base pairs 50,347,487 to 50,351,055 on chromosome 3 (Homo sapiens Annotation Release 108, GRCh38.p7) (NCBI)



Credit: Genome Decoration Page/NCBI

Other Names for This Gene

- NPR2
- NPR2-like protein
- NPR2L
- tumor suppressor candidate 4
- TUSC4

Additional Information & Resources

Educational Resources

- Jasper's Basic Mechanisms of the Epilepsies (fourth edition, 2012): mTOR and Epileptogenesis in Developmental Brain Malformations https://www.ncbi.nlm.nih.gov/books/NBK98145/

Scientific Articles on PubMed

- PubMed https://www.ncbi.nlm.nih.gov/pubmed?term=%28NPRL2%5BTIAB%5D%29+AND+%28%28Genes%5BMH%5D%29+OR+%28Genetic+Phenomena%5BMH%5D%29%29+AND+english%5Bla%5D+AND+human%5Bmh%5D+AND+%22last+3600+days%22%5Bdp%5D

OMIM

- NPR2-LIKE PROTEIN, GATOR1 COMPLEX SUBUNIT http://omim.org/entry/607072

Research Resources

- Atlas of Genetics and Cytogenetics in Oncology and Haematology
  http://atlasgeneticsoncology.org/Genes/GC_NPRL2.html
- ClinVar
  https://www.ncbi.nlm.nih.gov/clinvar?term=NPRL2%5Bgene%5D
- HGNC Gene Family: GATOR1 subcomplex
  http://www.genenames.org/cgi-bin/genefamilies/set/1394
- HGNC Gene Symbol Report
  http://www.genenames.org/cgi-bin/gene_symbol_report?q=data/hgnc_data.php&hgnc_id=24969
- NCBI Gene
  https://www.ncbi.nlm.nih.gov/gene/10641
- UniProt
  http://www.uniprot.org/uniprot/Q8WTW4

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